THL Psychiatric Family Collections

Information for researchers interested in using samples and data

Introduction

The THL Psychiatric Family Collections include families ascertained for schizophrenia (SZ), schizoaffective disorder and bipolar spectrum disorder (BPD). This large study was initiated in the 1990s with the aim of studying the genetic risk factors for serious psychiatric disorders. Families were recruited country-wide, and the diagnosis of each patient was reliably validated based on DSM-IV criteria.

A blood sample for DNA extraction has been collected from each participant (see Table 1 for details) and in addition a wide range of phenotypes, including neurocognitive tests, are available for both affected and unaffected family members.

This large family collection of schizophrenia and bipolar disorder patients and their 1st degree relatives is nationally and internationally valuable for the study of genetic risk factors associated with severe mental illness.

Ethical considerations

The study was approved by the Ministry of Social Affairs and Health (Finland) and the appropriate institutional review boards at the various stages of sample and data collections. The study was originally approved by the Ethics Committee of the National Public Health Institute (currently THL) on 16 May 1994, and later on 30 December 1998. Additional sample and data collection was approved by the Coordinating Ethical Committee of the Helsinki and Uusimaa Hospital Region on 9 December 2005. All participants have signed an informed consent that permits the use of collected samples and data for the study of the genetics of psychiatric disorders.

The THL Psychiatric Family Collections have been transferred to THL Biobank in 26 May 2015, following a public announcement that appeared in the Official Newspapers on 25 March 2015. THL Biobank hosts samples and data only from individuals who have donated samples, signed informed consent and who have not prohibited the transfer of their samples and data to THL Biobank. The transfer of the THL Psychiatric Family Collections to the biobank has been approved by the Coordinating Ethics Committee of Helsinki University Hospital on 10 October 2014 and by the Ministry of Social Affairs and Health on 9 March 2015. Also in THL Biobank, the samples and data can be used only for the study of psychiatric disorders.

Schizophrenia Family Sample (FSZ)

The SZ family sample is a systematically collected sample of Finnish SZ families. Families were identified through a search of nationwide health care and population registries. All individuals born in Finland between 1940 and 1976 (inclusive) were screened for hospitalization during the period from 1969 to 1998 (Hospital Discharge Register), for use of free antipsychotic medication (Medication Reimbursement Register), or disability pension (Pension Register) due to SZ, schizoaffective disorder, or schizophreniform disorder. Pedigrees were constructed by linking the unique identification numbers of the affected to their family members, derived from the Population Register Center.

Two different sets of SZ families were recruited for the study:

1) Families with at least two siblings with SZ and their first-degree relatives from the whole geographical area of Finland (2/3 of the families)
2) Families with at least one SZ patient from an isolated region in the north-eastern part of the country (Kuusamo) in which a higher lifetime morbid risk of SZ (3.2% vs. 1.1% in the total Finnish population) is present (1/3 of the families).

Bipolar Family Sample (BPD)

The Bipolar Family Sample was collected by combining information from the Finnish National Hospital Discharge Register to that from the National Population Register to construct families with high familial loading of BPD. First, all individuals that were born between the years 1940-1969 and hospitalized for ICD-defined BPD, were identified through the National Hospital Discharge Register. First-degree relatives were identified by linking the data to the National Population Register. Probands were recruited for study if they answered the following additional criteria: onset of disease before the age of 30 with two or more hospital admissions due to BPD, and in addition, the probands had to have at least one sibling. Also, at least one of the parents had to be born in the Eastern part of Finland where BPD seemed to be enriched.

In addition to the original BPD sample set, eight bipolar families were identified among the FSZ families. Also, the Finnish Twin Cohorts were used to identify twins in which at least one was affected with BPD, and 62 BPD twin pairs were recruited for the study. The bipolar family samples consist of 180 families.

Five hierarchical diagnostic categories were assigned to the affected individuals: 1. bipolar disorder type I; 2. schizoaffective disorder, bipolar type; 3. bipolar disorder type II, bipolar NOS, cyclothymia; 4. recurrent major depressive disorder; 5. other mental disorders. Before the year 1987 the diagnoses were made using the International Classification of Disease, version 8 (ICD-8) and starting from 1987 the diagnosis was coded according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, revised third edition (DSM-III-R).

FSZ and BPD samples and omics data available for biobank research

Table 1 provides information on the samples and omics data available from THL Psychiatric Family Collections.

Table 1. Basic information of the schizophrenia and bipolar disease sample collections

Sample collection	# families	# participants	Collected samples	# DNA sample donors	Other samples	Collection years	Omics data
FSZ[1]	734	3405	EDTA-Blood	3405	RNA samples[3], B-cell lines(subset)	1994-2008	SNP GWAS, Exome-seq., Transcriptomics[3]
BPD[2]	180	678	EDTA-Blood	678	B-cell lines(subset)	1994-2004	SNP GWAS

[1] Schizophrenia Family Sample, [2] Bipolar Disease Family Sample,

[3] Illumina HumanHT-12 v4 Expression BeadChip genome-wide gene expression data for 65 individuals from 18 families of the Finnish Schizophrenia Family Study. Reference: Stoll G, Pietiläinen OP et al. Deletion of TOP3β, a component of FMRP-containing mRNPs, contributes to neurodevelopmental disorders. Nat Neurosci. 2013 Sep;16(9):1228-37.

FSZ and BPD phenotype data available for biobank research

Data available for **all/most individuals** in the study:

- Basic information (age, sex)
- Family structures

Data available for **affected individuals** only:

- Best-estimate lifetime diagnoses assessed according to the DSM-IV criteria (Method: Two psychiatrists independently determined the consensus best estimate lifetime diagnosis, based on all available case reports, blind to family structure and register diagnosis. If these two psychiatrists provided conflicting diagnoses a third independent psychiatrist was used to reach the consensus.)
- Operational Criteria (OPCRIT) 90 item checklist (McGuffin et al., 1991), filled by a psychiatrist

Additional cognitive data and endophenotypes are available for 929 FSZ individuals (29% from all Finland and 71% from the internal isolate) and for 159 BPD individuals (65 families). These data are available for both **affected and unaffected individuals** and include:

- Structured Clinical Interview for DSM-IV (SCID-I) (First et al. 1997)
- Structured Clinical Interview for DSM-IV (SCID-II) for participants without psychotic disorder (First et al. 1997)
- Schedules for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1984) for affected individuals
- Schedules for the Assessment of Negative Symptoms (SANS) (Andreasen, 1983) for unaffected individuals
- Cognitive measurements (administered by psychologists or trained research nurses):
    - Vocabulary subtest of Wechsler Adult intelligence Scale-Revisited (WAIS-R)
    - Digit Span forward and backward test of the Wechsler Memory Scale-Revisited (WMS-R)
    - Digit Symbol subtest of WAIS-R
    - Visual Span forward and backward subtests of WMS-R
    - California Verbal Learning Test
    - Stroop task and Trail Making Test (TMT)

Registry data

Information from the Finnish national health registries, such as Care Register for Health Care (HILMO), Cancer Register, Cause-of-Death Register and Drug Imbursement Registers etc., can be linked to sample donors by separate application process.

Research group

Principal Investigators

Schizophrenia – Professor Jouko Lönnqvist, THL
Schizophrenia (clinical) – Professor Jaana Suvisaari, THL
Bipolar (clinical) – Professor Timo Partonen, THL
Schizophrenia and Bipolar (genetics) – Professor Tiina Paunio, THL

Key references

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